

Note on the physical basis of spatially resolved thermodynamic functions

Rasmus A. X. Persson¹

Department of Chemistry & Molecular Biology, University of Gothenburg, SE-412 96 Göteborg, Sweden^{a)}

The spatial resolution of thermodynamic functions, exemplified by the entropy, is discussed. A physical definition of the spatial resolution based on a spatial analogy of the partial molar entropy is advocated. It is shown that neither the grid cell theory (Gerogiokas *et al.*, J. Chem. Theory Comput., 10, 35 [2014]), nor the first-order grid inhomogeneous solvation theory (Nguyen *et al.*, J. Chem. Phys., 137, 044101 [2012]), of spatially resolved hydration entropies satisfies the definition.

Consider a system with N interacting molecules in equilibrium. Expressed in the N spatial position vectors $\{\mathbf{r}_i\}_{i=1}^N$, the (configurational) Gibbs equilibrium entropy of the system is

$$S_{\text{tot}} = - \int d^3\mathbf{r}_1 \dots d^3\mathbf{r}_N p(\{\mathbf{r}_i\}) \ln p(\{\mathbf{r}_i\}) \quad (1)$$

where $p(\{\mathbf{r}_i\})$ is the equilibrium distribution function of the molecule coordinates. S_{tot} is a function of external parameters (*e. g.*, pressure or temperature) but not of the molecule coordinates. In this Note, we discuss the *spatial* decomposition of thermodynamic functions, exemplified by the entropy in eq. (1). In this case, a local entropy density that depends on the spatial location, in addition to the external parameters, is introduced.

Mark and van Gunsteren¹ criticized any attempt at decompositions of the entropy (or free energy) in terms of particular atomic interactions for non-ideal systems. Nevertheless, as of recently, several authors²⁻⁹ have studied decompositions of S_{tot} of the form,

$$S_{\text{tot}} = \int d^3\mathbf{x} \bar{S}(\mathbf{x}) \quad (2)$$

where $\bar{S}(\mathbf{x})$ is the *local* entropy density at position \mathbf{x} in the system. For inhomogeneous systems (*e. g.*, a solute in solvent), these authors claim that such an analysis provides important physical insight. However, it should be clear that eq. (2) may be exactly satisfied by an infinite number of different choices for the function $\bar{S}(\mathbf{x})$. Consequently, there would seem to be an infinite number of different “insights” to be gained from the corresponding plethora of different decompositions. However, in certain cases physical conditions narrow the number of permissible decompositions. For instance, the translational symmetry of the homogeneous fluid imposes the condition that the gradient of $\bar{S}(\mathbf{x})$ vanish in that case. More generally, for two points \mathbf{x}_1 and \mathbf{x}_2 equivalent by symmetry, we have $\bar{S}(\mathbf{x}_1) = \bar{S}(\mathbf{x}_2)$. Such symmetry conditions are, however, generally not sufficient to uniquely define the function $\bar{S}(\mathbf{x})$ except in the homogeneous case, and they are likely to be trivially satisfied otherwise.

To exemplify the pitfalls, consider one intuitive contender for the local entropy density (δ denotes Dirac’s delta-

function):

$$\tilde{S}(\mathbf{x}) = - \int d^3\mathbf{r}_1 \dots d^3\mathbf{r}_N p(\{\mathbf{r}_i\}) \ln p(\{\mathbf{r}_i\}) \sum_{i=1}^N \delta(\mathbf{r}_i - \mathbf{x}) \quad (3)$$

where it is clear that one recovers the Gibbs entropy (eq. [1]) by integrating $\tilde{S}(\mathbf{x})$ over all space. However, there is no clear physical meaning ascribable to $\tilde{S}(\mathbf{x})$. If in an overall inhomogeneous system—say, the solvent around a solute—one computes $\tilde{S}(\mathbf{x})$ at a point far from any inhomogeneity, does one obtain the bulk molar (configurational) entropy of the solvent? This is a reasonable further physical condition that the physical entropy density function should satisfy. In fact, if this condition is fulfilled, a direct corollary of eq. (2) is that the entropy of solvation of a monoatomic solute may be computed as

$$\Delta S_{\text{tot}} = \int d^3\mathbf{x} [\bar{S}(\mathbf{x}) - \bar{S}_{\infty}] \quad (4)$$

where \bar{S}_{∞} is the entropy density function evaluated for the bulk solvent (infinitely removed from the solute). The question is what physical interpretation can be ascribed to the integrand $\bar{S}(\mathbf{x}) - \bar{S}_{\infty}$.

Because of correlations, the individual volume elements of the fluid are not independent subsystems. If they had been, the extensivity of the entropy would imply a linear dependence on the number of molecules in the subsystem—at *fixed* pressure P and temperature T —and the local entropy at a point could be obtained by the change in total entropy upon addition of extra molecules at that point. Extending this reasoning to the interacting subsystems, we deal with an infinitesimal change, so the local entropy at position \mathbf{x} is

$$\left(\frac{\partial S_{\text{tot}}}{\partial N(\mathbf{x})} \right)_{T,P},$$

and the entropy *density* of eq. (2) becomes:

$$\bar{S}(\mathbf{x}) = \rho(\mathbf{x}) \left(\frac{\partial S_{\text{tot}}}{\partial N(\mathbf{x})} \right)_{T,P} \quad (5)$$

Here $\rho(\mathbf{x})$ and $N(\mathbf{x})$ denote, respectively, the number density and number of molecules at position \mathbf{x} , both of which are fluctuating quantities: appropriate ensemble averaging is implicitly understood for both (and so $N(\mathbf{x})$ is not necessarily integer). This choice for $\bar{S}(\mathbf{x})$ is obviously unique and satisfies the symmetry constraints. Moreover, eq. (2) is satisfied as

^{a)}Electronic mail: rasmus.a.persson@gmail.com

well. This can be seen by using a discrete approximation for $\rho(\mathbf{x})$ in which space is divided into M cells, indexed by i , of a small but finite volume V , writing

$$\bar{S}_i = \frac{N_i}{V} \left(\frac{\partial S_{\text{tot}}}{\partial N_i} \right)_{T,P} \quad (6)$$

where N_i is the number of molecules in cell i . From this, we have the differentials

$$dS_{\text{tot}} = \sum_i^M \left(\frac{\partial S_{\text{tot}}}{\partial N_i} \right)_{T,P} dN_i \quad (7)$$

and

$$d\bar{S}_i = \frac{dN_i}{V} \left(\frac{\partial S_{\text{tot}}}{\partial N_i} \right)_{T,P} \quad (8)$$

which combined lead to a discrete analog of eq. (2). The physical interpretation of the integrand in eq. (4) according to eq. (5) should be clear. The difference $(\bar{S}(\mathbf{x}) - \bar{S}_\infty)d^3\mathbf{x}$ is the infinitesimal change in total entropy of transforming the (solvent) density at \mathbf{x} from bulk density to $\rho(\mathbf{x})$: the space integral over all these rearrangements yields the total entropy change.

We now consider the extent to which the entropy of grid cell theory⁴ (GCT; a spatially resolved variant of Henchman's cell theory¹⁰) conforms to eq. (5), in which we replace the Gibbs entropy by its GCT approximation $S_{\text{tot}}^{\text{GCT}}$. In this theory, the configuration space is divided into discrete cells and the average magnitude of the force of every molecule within a specific cell is computed. The local entropy density of the cell is then computed as,¹¹

$$\bar{S}_i^{\text{GCT}} = \frac{N_i}{V} S_i^{\text{HO}} \quad (9)$$

where S_i^{HO} is the entropy of the harmonic oscillator whose average force magnitude f_i equals that of cell i : $S_i^{\text{HO}} \propto \ln f_i$. To compute spatially resolved entropies of hydration, Gerogiokas *et al.*⁴ apply a version of eq. (4). Whether eq. (5) is satisfied or not within GCT is thus of some interest.

Since the total entropy is taken as (to satisfy eq. [2])

$$S_{\text{tot}}^{\text{GCT}} = \sum_j^M N_j S_j^{\text{HO}} \quad (10)$$

then $S_i^{\text{HO}} = (\partial S_{\text{tot}}^{\text{GCT}} / \partial N_i)_{T,P}$ only if

$$\sum_{j \neq i} N_j \left(\frac{\partial S_j^{\text{HO}}}{\partial N_i} \right)_{T,P} = -N_i \left(\frac{\partial S_i^{\text{HO}}}{\partial N_i} \right)_{T,P} \quad (11)$$

Let us for simplicity examine this equation in the special case of a system that is divided into two grid cells that together contain all of the molecules in the system. With this simplification, and the chain rule for derivatives, eq. (11) may then be cast as

$$\frac{N_2}{f_2} \left(\frac{\partial f_2}{\partial N_1} \right)_{T,P} = -\frac{N_1}{f_1} \left(\frac{\partial f_1}{\partial N_1} \right)_{T,P} \quad (12)$$

where $f_1, f_2 \geq 0$ are the average *magnitudes* of the force in cell 1 and 2, respectively, and $N_1, N_2 \geq 0$ are the corresponding numbers of molecules. Clearly, consistency with eq. (11) requires that the change in the average *magnitude* of the force in one cell is opposite in sign to the corresponding change in the other cell. However, in an inertial reference frame, the total force vanishes. Therefore, the *force* in cell 1 always cancels that in cell 2. Hence, an increase in the average *magnitude* of the force in one cell must be accompanied by an increase of the average *magnitude* also in the other cell, which contradicts eq. (12). Eq. (11) is thus disproved.

While not based directly on eq. (4), it is nevertheless instructive to investigate to what extent the spatially resolved hydration entropy, computed by first-order grid inhomogeneous solvation theory (GIST) in Ref. 2, satisfies eq. (5). In the present notation (Boltzmann constant set to unity), the first-order local GIST solvation entropy density is written,¹²

$$\Delta \bar{S}_i^{\text{GIST}} = -\frac{N_i}{V} \ln \left(\frac{N_i}{V \rho_\infty} \right) \quad (13)$$

where ρ_∞ is the bulk density, and so (V implicitly depends on N_i due to the condition of constant pressure)

$$\left(\frac{\partial \Delta \bar{S}_i^{\text{GIST}}}{\partial N_i} \right)_{T,P} = - \left[\ln \left(\frac{N_i}{V \rho_\infty} \right) + 1 - \frac{N_i}{V} \left(\frac{\partial V}{\partial N_i} \right)_{T,P} \right] \quad (14)$$

which proves that eq. (5) is not satisfied save for an ideal gas (for which $(\partial V / \partial N_i)_{T,P} = V / N_i$).

It has been the purpose of this Note to highlight the problem of interpretation of spatially resolved thermodynamic functions, in particular the equilibrium entropy, and also to offer a physical definition, free of any model assumptions, which in principle can be measured, albeit not in practice outside of the computer simulation. I believe that only with a solid physical basis is the analysis of spatially resolved thermodynamics edifying. Of note is the isomorphism between eq. (5) and the partial molar entropy in the theory of mixtures. In light of eq. (5), each molecule may be taken to be its own species, identified by its physical location. Diffusion of molecules throughout the fluid is then analogous to chemical interconversion. This analogy is also the basis of the anisotropic extension of integral equation theories for fluids.¹³

¹A. E. Mark and W. F. van Gunsteren, J. Mol. Biol. **240**, 167 (1994).

²C. N. Nguyen, T. K. Young, and M. K. Gilson, J. Chem. Phys. **137**, 044101 (2012).

³E. P. Raman and A. D. MacKerell Jr, J. Chem. Phys. **139**, 055105 (2013).

⁴G. Gerogiokas, G. Calabro, R. H. Henchman, M. W. Southey, R. J. Law, and J. Michel, J. Chem. Theory Comput. **10**, 35 (2013).

⁵C. N. Nguyen, A. Cruz, M. K. Gilson, and T. Kurtzman, J. Chem. Theory Comput. **10**, 2769 (2014).

⁶J. Michel, R. H. Henchman, G. Gerogiokas, M. W. Southey, M. P. Mazanetz, and R. J. Law, J. Chem. Theory Comput. **10**, 4055 (2014).

⁷G. Gerogiokas, M. Southey, M. Mazanetz, A. Hefetz, M. Bodkin, R. Law, and J. Michel, Phys. Chem. Chem. Phys. **17**, 8416 (2015).

⁸C. N. Nguyen, T. Kurtzman, and M. K. Gilson, J. Chem. Theory Comput. (2015).

⁹E. P. Raman and A. D. MacKerell Jr, J. Am. Chem. Soc. **137**, 2608 (2015).

¹⁰R. H. Henchman, J. Chem. Phys. **119**, 400 (2003).

¹¹For notational simplicity, we only consider the translational contribution, as we have only dealt with monoatomic molecules elsewhere.

¹²Only the translational contribution is considered.

¹³R. Kjellander and S. Marčelja, J. Chem. Phys. **82**, 2122 (1985).